REMARKS

I. Support for Amendments

A new abstract on a separate sheet of paper was submitted in order to comply with 37 CFR 1.72(b) as pointed out by the Examiner. Figure 1 was amended in order to add a previously omitted element identifier and Figure 3 was amended to correct a typographical error for an element identifier. Claims 1-2, 4, 9-10, and 13 were canceled, new claims 21-23 were added, and claims 3, 5-8, 11-12, 14-17, and 20 were amended to more clearly define the claimed invention and correct dependency. Support for the newly added claims and amendments is found throughout the Specification, for example, on page 5, lines 17-28, page 7, line 14, page 8, lines 9-10, page 11, line 13, page 16, lines 14-17, and page 19, line 22 to page 20, line 3. Accordingly, no new matter is added by this Amendment and entry thereof is respectfully requested.

II. Objection to Claim 8

The Examiner objected to claim 8 under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the scope of the previous claim. Claim 8 has been amended to correct this improper form and withdrawal of the rejection is, therefore, respectfully requested.

III. Objections to the Specification

The Examiner objected to the specification because it did not contain an abstract of the disclosure as required by 37 CFR 1.72(b). Applicants file herewith an abstract on a separate sheet of paper. Accordingly, withdrawal of this objection is respectfully requested.

The Examiner also objected to the specification by asserting that it failed to provide a proper antecedent basis for the claimed subject matter of claim 11. Claim 11 has been amended to more clearly define the invention so that the antecedent rejection is no longer applicable. Accordingly, withdrawal of this objection is respectfully requested.

IV. Rejection of claims 1-20 under 35 U.S.C. 112, second paragraph

The Examiner has rejected claims 1-20 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 1, 9, and 10 were rejected as being incomplete for omitting essential steps. These claims have been canceled. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1 and 9 were also rejected under 35 U.S.C. §112, second paragraph, as the Examiner asserts that the term "large" is a relative term that renders the claim indefinite. These claims have been canceled and withdrawal of the rejection is, therefore, respectfully requested.

The Examiner also rejected claims 2-4 as being indefinite by asserting that the claims do not set forth any steps involved in the method/process rendering it unclear as to what

method/process applicant is intending to encompass. Applicants respectfully disagree. The necessary elements of the method are recited in claim 3, which depends from new claim 21. Claims 2 and 4 have been canceled and claim 3 has been amended to more clearly illustrate its dependency on the high-throughput method of claim 21. Accordingly, withdrawal of this rejection is respectfully rejected.

Claim 6 was also rejected for being indefinite as the Examiner asserts that the limitation of "said target" has insufficient antecedent basis. This claim has been amended to recite "at least one target molecule." Withdrawal of the rejection is respectfully requested.

Similarly, the Examiner rejected claim 10 by asserting that the limitation "said tissue sample" has insufficient antecedent basis. This claim has been canceled. Withdrawal of this rejection is respectfully requested.

Claim 11 was rejected because the Examiner asserts that it is unclear as to why the limitation of "a plurality of different oligonucleotides mounted to a solid support" is included. Claim 11 has been amended to more clearly define the invention. Accordingly, withdrawal of this objection is respectfully requested.

The Examiner also rejected claims 15 and 16 by asserting that the limitation of "the apparatus" has insufficient antecedent basis and because, as product claims, they improperly depend on a method claim. These claims have been amended to recite "the method" rather than "the apparatus." Accordingly, withdrawal of the rejection is respectfully requested.

Claim 17 was also rejected as the Examiner asserts that the limitation of "said machine" has insufficient antecedent basis. This claim has been amended to recite a "staining instrument" rather than "said machine." Withdrawal of the rejection is, therefore, respectfully requested.

V. Rejection of claims 2-4 under 35 U.S.C. § 101

Claims 2-4 were rejected under 35 U.S.C. § 101 as the Examiner asserts that the claimed recitation of use, without setting forth any steps involved in the process, results in an improper definition of a process and results in a claim which is not a proper process claim under 35 U.S.C. 101. Claims 2 and 4 have been canceled and claim 3 has been amended so that its dependency on the method of claim 21 is clearly stated. Accordingly, withdrawal of this rejection is respectfully requested.

VI. Rejection of claims 1-13 and 17-20 under 35 U.S.C. § 103(a)

Claims 1-13 and 17-20 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Leighton (U.S. Patent No. 6,103,518), in view of Kalra et al. (U.S. Patent No. 6,495,106). Leighton is relied on in this Action for teaching a method for evaluating the clinical utility of target molecules comprising the steps of providing a large quantity of different tissue samples, providing a target molecule, providing a stain that specifically binds to said target molecule *in situ,* applying said stain to said tissue samples and determining the extent to which said stain has bound to said target molecule in said tissue samples. Kalra et al. is relied on for teaching that modern laboratories find it desirable to automate the staining process in order to examine large numbers of tissue specimens.

The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use an automated stainer to stain the tissue samples in a high-throughput manner in the method disclosed by Leighton, in order to examine large numbers of tissue specimens. Applicants respectfully traverse this rejection because claims 1-

13 and 17-20, are not obvious in view of the Leighton and Kalra et al. for the reasons discussed below.

First, Applicants respectfully assert that the Kalra et al. reference is not appropriate prior art with regard to the current application. According to the MPEP § 706.02(f)(l), the 35 U.S.C. § 102(e) date of a U.S. patent based on an international application filed prior to November 29, 2000 is the same as the §371(c)(1),(2), (4) date. The Kalra et al. PCT application was filed on March 24, 1998 (prior to the Nov. 29, 2000 effective date of the amended § 102(e)), and its §371(c)(1),(2),(4) date is Dec. 15, 2000. The current application claims priority to Provisional Application No. 60/155,665, which was filed on September 24, 1999. Therefore, the Kalra et al. patent cannot be cited against the current application as prior art and the rejection is improper. While Kalra is not prior art, in the interest of moving prosecution forward, Applicants address the Leighton patent herein.

To properly make a rejection under 35 U.S.C. § 103, the Examiner has the initial burden of establishing *a prima facie* case of obviousness. Meeting this burden requires the Examiner to show first, that the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process. Second, the Examiner must establish that the prior art would have revealed that in so making or carrying out the claimed process, those of ordinary skill in the art would have had a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art, not in Applicants' disclosure. *In re Vaeck,* 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.,* 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

The Leighton patent does not teach or suggest a high-throughput method for evaluating the clinical utility of target molecule(s) using a plurality of tissue microarrays as recited in new claims 21-22. In addition, Leighton does not teach or suggest an instrument for automatically applying said stain to said tissue sample as recited in new claim 23. Rather, Leighton utilizes a single tissue microarray and does not utilize an automated staining process as claimed herein. There is no teaching or suggestion to utilize more than one tissue microarray at any one time. Therefore, there is no suggestion to conduct the high-throughput method of evaluating the clinical utility of at least one target molecule using a plurality of tissue microarrays and further utilizing an automated staining process, as claimed herein. Applicants respectfully request that the rejection be withdrawn.

With respect to claims 2 and 4, these claims have been canceled, rendering this rejection moot. Accordingly, withdrawal of this rejection is respectfully requested.

With respect to claim 3, the Examiner asserts that Leighton teaches the staining of tissue samples to reveal structures of interest. Since claim 3 is dependent upon new claim 21, the method of claim 3 would not have been obvious to one of skill in the art over Leighton because of the reasons discussed above. In addition, as the Examiner states, Leighton does not teach the use of an automated stainer as recited in claim 3. As stated above, Kalra et al. is not prior art with regard to the current application. Therefore, Applicants respectfully request that the rejection be withdrawn.

The Examiner also asserts that claims 5-8, and 11-13 are obvious over Leighton in view of Kalra et al. Since claims 5-8 depend upon newly added claim 21 and claims 11-12 depend upon newly added claim 23, these claims are not obvious over the Leighton patent for the

reasons discussed above. Furthermore, claim 13 has been canceled. Applicants, therefore, respectfully request that the rejection be withdrawn.

With respect to claims 17-20, the Examiner asserts that these claims are obvious over Leigton in view of Kalra et al. Leighton is relied on in this Action for teaching a tissue microarray that has a solid surface with tissue samples mounted to the solid surface. As stated by the Examiner, Leighton does not teach the use of the bar code labeled slide for identifying how the tissues are to be treated by a machine as recited in claims 17-19. As further stated by the Examiner, Leighton does not teach a treatment comprising automated staining of tissues as recited in claim 20. Hence, these claims are not obvious in view of Leighton and withdrawal of the rejection is respectfully requested.

VII. Rejection of claims 14-16 under 35 U.S.C. § 103(a)

The Examiner has rejected claims 14-16 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Leighton (U.S. Patent No. 6,103,518), in view of Kalra (U.S. Patent No. 6,495,106) as applied to claims 1-13, and 17-20, and further in view of Bogen et al. (U.S. Patent No. 6,183,693). Applicants respectfully traverse this rejection and submit that claims 14-16 are not obvious in view of Leighton, in view of Kalra, further in view of Bogen et al. for the reasons discussed below.

As explained above, Leighton is relied on in this Action for teaching a method for evaluating the clinical utility of target molecules comprising the steps of providing a large quantity of different tissue samples, providing a target molecule, providing a stain that specifically binds to said target molecule *in situ,* applying said stain to said tissue samples and

determining the extent to which said stain has bound to said target molecule in said tissue samples. Bogen et al. is relied on for teaching that various staining procedures require heat at different times to enhance the rate of chemical reaction; therefore, a means has developed to heat slides to different temperatures, independently of the temperature of the other slides. The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use an instrument with multiple heaters in the method of Leighton, as taught by Bogen, in order to enhance the rate of chemical reaction during staining. Applicants respectfully traverse this rejection because claims 14-16 are not obvious in view of Leighton in view of Kalra et al., further in view of Bogen et al. for the reasons discussed below.

Since claims 14-16 depend upon newly added claim 23, they are not obvious over the Leighton patent for the reasons discussed above. Specifically, Leighton does not teach a high-throughput method of evaluating a target molecule for clinical utility, as claimed herein. In addition, as explained above, the Kalra et al. patent is not appropriate prior art in view of the priority date of the current application. Furthermore, the Bogen patent does not remedy the deficiencies of the Leighton patent in that it does not teach or suggest a high-throughput method for determining whether a target molecule has clinical utility by providing an instrument for automatically applying said stain to said tissue sample, wherein said target molecule was identified using an array as recited in claim 23.

Accordingly, the combination of the Leighton and Bogen references does not teach or suggest the presently claimed invention. Applicants respectfully request that this rejection of claims 14-16 be withdrawn.

VIII. CONCLUSION

In view of the foregoing remarks, Applicants believe that the application is in condition for allowance. However, if the Examiner disagrees, he is encouraged to call the undersigned at the number listed below in order to expedite the prosecution of this application.

Respectfully submitted,

#38,898 for

Maria L. Maebius
Attorney for Applicant
Reg. No. 42,967

Date: 3/22/2004

Hale and Dorr LLP
1455 Pennsylvania Ave., NW
Washington, D.C. 20004
(202) 942-8452